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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,726	08/29/2003	Chihiro Uematsu	1021.43085X00	9438

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EXAMINER	
BABIC, CHRISTOPHER M	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 06/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/650,726	UEMATSU ET AL.	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-5 is/are pending in the application.

4a) Of the above claim(s) 6 and 7 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-5 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-7 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/29/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.00

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-5, drawn to a method for gene expression classified in class 435, subclass 91.2, for example.

II. Claims 6 and 7 drawn to a kit for gene expression classified in class 530, subclass 24.3, for example.

The inventions are distinct, each from the other because of the following reasons:

Inventions II and I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the process of Group I as limited by Claim 1 can be accomplished with multiple materially different primers that are outside the scope of the kit of Group II, for example.

Furthermore, searching the inventions of Groups I and II together would impose serious search burden. The inventions of Groups I and II have obtained a separate status in the art as shown by their different classifications. Moreover, since the process of the independent claim of Group I (Claim 1) does not require the products of Group II, the search of these groups together is not coextensive. A search for the process of

Claim 1 would not necessarily result in any of the products of Group II. As such, it would be burdensome to search the inventions of Groups I and II together.

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

During a telephone conversation with William Solomon on June 10, 2005, a provisional election was made without traverse to prosecute the invention of Group I (Claims 1-5). Affirmation of this election must be made by applicant in replying to this Office action. Claims 6 and 7 are hereby **withdrawn** from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to

be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 3 recite the limitation "the third base sequence" in line 4 of Claim 2 and line 5 of Claim 3. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Whitcombe et al. (WO 97/42345).

These claims are drawn to a method for gene expression analysis comprising: subjecting a gene to be analyzed to nucleic acid amplification in a single thermal cycle

using a primer comprising a base sequence specifically hybridizing to a target gene, a primer comprising a base sequence identical to a second base sequence, a probe comprising a base sequence identical or complementary to a first base sequence, and labeled at one end with a fluorophore and at another end with a quencher, and thermostable DNA polymerase having 5'-3' exonuclease activity, digesting the probe hybridized to the first base sequence by the thermostable DNA polymerase at the time of the nucleic acid amplification, and detecting a fluorescence emitted by the released fluorophore, thereby assaying the amount of the product of the nucleic acid amplification, wherein the gene to be analyzed is prepared by introducing the first base sequence and the second base sequence, which are nonspecific to the base sequence of the target gene, into the target gene so that the second base sequence is bound to a position closer to the 5' end than the first base sequence.

Regarding Claim 1, Whitcombe et al. disclose an assay system for the detection of diagnostic base sequences which use tailed diagnostic primers having a tag region and detector region (Abstract; Page 1, Lines 20-23; Figures 9a, 9b, 10a, 10b, 10c; Page 16, Example 1; Pages 19-23, Results Section). They disclose an amplification procedure where primer extension products are amplified using a further primer (Page 4, Lines 1-7; Page 20, Results Section, Examples 1, 2, 3). They disclose diagnostic primers which are genome specific at their 3'-termini but which carry detector region and common extension tags (tags) at their 5'-termini (Page 4, Lines 22-25; Figure 9a; Page 17, Example 1, Lines 18-24). They teach that a labeled hybridization detector probe, specifically those having interactive labels (i.e. FRET, Fluorescence Resonance

Energy Transfer), may be used with their invention in association with exonuclease activity of a polymerase mediated extension reaction (Page 2, Lines 23-29; Figures 10a, 10b, 10c). They teach preparation of a target gene using their aforementioned diagnostic primers (Page 4, Lines 1-7; Figure 9a).

Regarding Claim 2, Whitcombe et al. disclose the preparation of a target gene using their aforementioned diagnostic primers (Page 4, Lines 1-7; Figure 9a).

Regarding Claim 3, Whitcombe et al. disclose their invention as being well suited for homogeneous assays and real time or end point analysis (Page 2, Lines 17-18). It is inherent to one of ordinary skill in the art that "real time or end point analysis" encompasses quantification of mRNA by using a reverse transcriptase PCR reaction to prepare cDNA for experimentation (For example, please see included reference: Overbergh et al. Quantification of Murine Cytokine mRNAs Using Real Time Quantitative Reverse Transcriptase PCR. Cytokine, Vol. 11, No. 4. April, 1999: 305-312).

Regarding Claim 4, Whticombe et al. disclose the use of their invention with the Amplification Refractory Mutation System (ARMS) in a multiplex single tube genotyping assay where multiple probes are utilized in one reaction vessel.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Whitcombe et al. (WO 97/42345), in view of Shah et al. (U.S. 6,165,723).

This claim is drawn to the methods presented in Claims 1 and 4, wherein the T_m values of the two or more types of probes are substantially the same.

The methods disclosed by Whitcombe are discussed in the previous rejections. Whitcombe et al. does not specifically teach a multiplex assay with multiple probes having substantially the same T_m value.

Shah et al. disclose an in situ hybridization method for detecting target nucleic acids, wherein for simultaneous detection the oligonucleotides which are specific for the different nucleic acids commonly present in the clinical specimen can be designed such that the T_m values of all probe complex sequences are very similar (Abstract; Column 5,

Lines 1-18). In addition, Shah et al. disclose several advantages of their methods, such as reduction hybridization time (Column 5, Lines 58-67).

One of ordinary skill in the art would have been motivated to use the probes disclosed by Shah et al. in the diagnostic amplification methods disclosed by Whitcombe et al. for among other advantages, a reduction in hybridization time. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods.

Conclusion

No claims are allowable. No claims are free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CMB

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